REMARKS

Claims 1-8, 10-19, 21-45, 47, 49-61 are pending. Claims 1, 2, 5, 6, 8, 10, 11, 18, 21 and 22 have been amended, claims 9 and 20 have been cancelled and claims 59-61 have been added.

No new matter has been added by way of the present Amendment. For example, Applicant has amended claim 1 to recite the hybridization conditions as supported by the present specification at page 5, line 27 to page 6, line 3. Claim 2 has been amended to recite "at least 90% homologous" as supported by the originally filed claim. Claims 1, 5, 6, 8 and 19 have been amended to remove the recitation of "or a sub-sequence thereof." The dependency of claims 10, 11, 21 and 22 has been altered as necessitated by the cancellation of claims 9 and 20. The preamble of claim 18 has been amended to recite "An isolated cell." New claim 59 is supported by originally filed claim 18 as well as the present specification at page 15, line 6 to page 16, line 17. New claim 60 is supported by originally filed claim 2. Lastly, new claim 61 is supported by the present specification at page 5, line 27 to page 6, line 3. Accordingly, no new matter has been added.

Applicant has attached a marked up version of the claims for the Examiner's consideration.

In view of the following remarks, Applicant respectfully requests that the Examiner withdraw all rejections and allow the currently pending claims.

Objection to the Title of the Invention

The Examiner has objected to the title of the invention asserting that it is not descriptive. Applicant respectfully traverses and submits that the new title of the invention has been submitted. Accordingly, this objection is moot. Reconsideration and withdrawal thereof are respectfully requested.

Issues under 35 U.S.C. §101

The Examiner has rejected claims 18-27 under 35 U.S.C. § 101 asserting that the claimed invention is non-statutory. Applicant respectfully traverses. Claim 18 has been amended to recite "an isolated cell". Accordingly, the Examiner may no longer construe these claims to read upon a human being. Reconsideration and withdrawal of this rejection are respectfully requested.

Issues under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 2, 9, 10, 11, 20, 21 and 22 under 35 U.S.C.§ 112, first paragraph for the reasons recited at pages 3-8 of the Office Action. Applicant respectfully traverses.

Concerning claims 9, 10, 11, 20, 21 and 22, Applicant submits that claims 9 and 20 have been cancelled, claims 10 and 11 now depend upon claim 7, and claims 21 and 22 now depend upon claim 18. Since the subject matter of claims 7 and 18 has not

been rejected under 35 USC § 112, first paragraph, the rejection concerning claims 9, 10, 11, 20, 21 and 22 is moot. Reconsideration and withdrawal thereof are requested.

Concerning the Examiner's rejection of claim 2, Applicant respectfully disagrees with the Examiner's reasoning. Applicant submits that the isolation of polynucleotides and polypeptides of sequences in addition to the ones presented in the Sequence Listing is in fact enabled by the present specification. Applicant has isolated and characterized a functional KCNQ4 subunit as disclosed in the specification. Applicant has also positively identified a variant polypeptide of physiological interest. Moreover, as disclosed in Table 1 of the present specification, Applicant has carried out an alignment of the present sequence with those of known polypeptides, thereby enabling the skilled person to introduce additional mutations in order to arrive at more variants of physiological interest. Because the conserved (*), semi-conserved (:) and lesser-conserved (.) regions are clearly identified in the Table, the specification provides sufficient guidance for the skilled person to arrive at the variants of interest with a reasonable expectation of success and without undue experimentation.

Based on the information provided in Table 1 and as discussed above, Applicant submits that the subject matter claimed is fully

enabled and described. Thus, Applicant is entitled to a scope broader than that defined by the specific sequences presented in the Sequence Listing.

In this respect we note that while the Examiner has found the subject matter of claim 1 to be fully enabled and described, he has rejected claim 2. There is, of course, a relationship between the degree of homology between two sequences and their ability to hybridize. The methods disclosed allow one of skill in the art to determine the bounds of the claims. Using the Blast 2 Sequences program provided by the National Center for Biotechnology Information (NCBI), and described by *Tatusova TA & Madden TL [Tatusova TA & Madden TL:* "Blast 2 sequences - a new tool *for* comparing protein and nucleotide sequences"; FEMS Microbiol. Lett., 1999 172 247-250), the homology (identity) between the KCNQ4 channel of the invention and the KCNQ1, KCNQ2 and KCNQ3 channels at amino acid level was calculated as 58%, 76% and 64%, respectively, On a nucleotide level the homology may be considerably lower. However, Applicant draws the Examiner's attention to the fact that claim 2 is limited to sequences that are "at least 90% homologous" to the sequence of SEQ ID NO:1

In view of the above as well as the disclosure of the present specification, Applicant respectfully submits that sufficient enablement and written description exists for the subject matter

of claim 2. Thus, the Examiner is requested to withdraw the rejection of claim 2 pursuant to 35 USC § 112, first paragraph.

The Examiner has also rejected claims 18-27 under 35 U.S.C. § 112, first paragraph asserting that the present specification, while being enabling for a host cell in culture, does not reasonably provide enablement for in vivo transfection. Applicant respectfully traverses and submit that claim 18 has been amended to recite "An isolated cell"; thus, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

Issues under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 1-11 and 18-30 under 35 U.S.C. § 112, second paragraph for the reasons recited at pages 8 and 9 of the outstanding Office Action. Applicant respectfully traverses.

First, Applicant submits that the "high stringency conditions" are now recited in claim 1. Second, the recitation of "sub-sequence" has been removed from the claims. Accordingly, these rejections are moot. Reconsideration and withdrawal thereof are respectfully requested.

Rejections under 35 U.S.C. § 102(b)

The Examiner has rejected claims 1, 3-11 and 18-30 under 35 U.S.C. § 102(b) as being anticipated by Singh et al. (1998). Applicant respectfully traverses this rejection.

The Singh reference discloses KCNQ2 cloned from a fetal brain cDNA library. As discussed above and in the present specification, the homology between the KCNQ4 channel of the present invention and the KCNQ2 channel of the same reference at the amino acid level was calculated as 76% homology. The KCNQ4 channel of the present invention is therefore distinguished over the KCNQ2 channel of the prior art. Thus, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

Issues under 35 U.S.C. § 103(a)

The Examiner has rejected claims 1, 3-11 and 18-30 under 35 U.S.C. § 103(a) as being obvious over Singh et al. in view of WO 9401548. Applicant respectfully traverses this rejection.

Applicant has explained above that the Singh reference discloses the KCNQ2 gene having less than 76% homology to the KCNQ4 gene of the present invention. Singh thus fail to suggest or disclose the subject matter currently claimed. Moreover, the WO 9401548 reference simply discloses human nucleic acid fragments isolated from brain adrenal tissue, placenta or bone

marrow. WO 9401548 fails to suggest or disclose any similarity between the sequences of present invention and those of Singh et al. Moreover, WO 9401548 fails to cure deficiencies of the Singh et al. reference. Accordingly, the Examiner's rejection under 35 U.S.C. § 103(a) is incorrect. Reconsideration and withdrawal thereof are respectfully requested.

In view of the above, Applicant respectfully submits that the present claims are in condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw all rejections and allow the currently pending claims.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Craig McRobbie (Reg. No. 42,874) at the telephone number of the undersigned below.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a one (1) month extension of time for filing a reply in connection with the present application, and the required fee of $$110.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____
Gerald M. Murphy, Jr., #28,977

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

GMM/CAM:bmp
2815-0127P

Attachment: Version with Markings to Show Changes Made

Rev. 09/26/01

VERSION WITH MARKINGS TO SHOW CHANGES MADE

The Title of the Invention:

The Title of the invention has been amended as follows:

--POTASSIUM CHANNELS AND GENES ENCODING THESE POTASSIUM CHANNELS--

IN THE CLAIMS:

Claims 9 and 20 have been canceled.

The claims have been amended as follows:

Claim 1. (Twice Amended) An isolated polynucleotide having a nucleic acid sequence which is capable of hybridizing under high stringency conditions with the polynucleotide sequence of SEQ ID No: 1, or its complementary strand, [or a sub-sequence thereof] wherein said hybridizing occurs in a solution of 5 x SSC, 5 x Denhardt's solution, 0.5% SDS and 100 µg/ml of denatured sonicated salmon sperm DNA for 12 hours at approximately 45°C followed by washing twice for 30 minutes in 2 x SSC, 0.5% SDS at a temperature of at least 65°C.

Claim 2. (Twice Amended) The isolated polynucleotide according to claim 1, wherein said isolated polynuclectide is at least [50% homologous, preferably more than 70% homologous, more preferably more than 80% homologous, even more preferably more than] 90% homologous[, and most preferably more than 95% homologous] to the polynucleotide sequence of SEQ ID NO:1.

Claim 5. (Twice Amended) The isolated polynucleotide according to claim 1, comprising the polynucleotide sequence of SEQ ID NO:1[, or a sub sequence thereof].

Claim 6. (Twice Amended) The isolated polynucleotide according to claim 1, comprising the polynucleotide sequence of SEQ ID NO:1, [or a sub sequence thereof,] wherein said sequence includes a mutation G935A.

Claim 8. (Twice Amended) The isolated polynucleotide according to claim 7, encoding a KCNQ4 potassium channel subunit comprising the amino acid sequence of SEQ ID NO:2[,or a sub sequence thereof].

Claim 10. (Twice Amended) The isolated [polynucletoide] polynucleotide according to claim [9] 7, wherein said variant has an amino acid sequence that has been changed at one or more positions located in a conserved region, wherein said region is defined by Table 1.

Claim 11. (Twice Amended) The isolated [polynucletoide] polynucleotide according to claim [9] 7, encoding a variant KCNQ4/G285S or KCNQ4/G333S when said polynucleotide is numbered according to KCNQ1.

Claim 18. (Twice Amended) [A] An isolated cell genetically manipulated by the incorporation of a heterologous polynucleotide according to claim 1.

Claim 19. (Twice Amended) The cell according to claim 18, genetically manipulated by the incorporation of a KCNQ4 channel subunit comprising the amino acid sequence of SEQ ID NO: 2[, or a sub-sequence thereof].

Claim 21. (Twice Amended) The cell according to claim [20] 18, wherein said variant has an amino acid sequence that has been changed at one or more positions located in a conserved region, wherein said region is defined by Table 1.

Claim 22. (Twice Amended) The cell according to claim [20] 18, genetically manipulated by the incorporation of the variant KCNQ4/G285S or KCNQ4/G333S when numbered according to KCNQ1.

Claims 59, 60 and 61 have been added.